Table 2. Associations of knee sagittal plane dynamic joint stiffness (DJS) during gait with knee pain assessed by WOMAC pain and by pain after 20-meter walk, stratified by gait speed regression coefficients (95% CI) (n=482 knees from 248 persons)

	WOMAC pain		Pain after 20-m walk	
	Speed > 1.20(n=230 knees)	Speed ≤1.20(n=252 knees)	Speed > 1.20(n=230 knees)	Speed ≤1.20(n=252 knees)
Unadjusted	−7.38* (−14.60,−0.17)	−0.75 (−8.19, 6.68)	−3.13* (−6.05, −0.21)	−0.38 (−3.88, 3.12)
Adjusted for age and gender	−6.13 (−12.90, 0.63)	2.20 (−5.64, 10.05)	−2.80 (−5.67, 0.07)	0.71 (−2.85, 4.26)
Adjusted for age, gender, K/L grade	−8.12* (−14.81,−1.43)	3.22 (−4.93, 11.37)	−3.44* (−6.52, −0.35)	0.22 (−3.45, 3.90)
Adjusted for age, gender, K/L grade, and strength	−7.14* (−13.37,−0.92)	4.35 (−3.25, 11.94)	−3.05* (−6.02, −0.08)	0.65 (−2.96, 4.26)

*95% CI excluding 0 is significant

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IN VIVO STRAIN INCREASES FOLLOWING MEDIAL MENISCAL TEAR AND CORRELATES WITH SYNOVIAL FLUID MATRIX METALLOPROTEINASE ACTIVITY

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Purpose: Abnormal cartilage loading is believed to play a role in the development of early onset osteoarthritis after meniscal injury. However, little is known regarding the precise mechanisms leading to osteoarthritis in this population. The goal of this study was to quantify the effects of meniscal tears on *in vivo* cartilage strains over a full range of weight bearing flexion angles and to determine the relationship of cartilage strain with biomarkers of cartilage degradation in the synovial fluid. We hypothesize that following a medial meniscus tear, the contact strain in the medial compartment will be increased, as compared to the uninjured knee, and that cartilage strain magnitudes will positively correlate with catabolic biomarkers in the synovial fluid.

Methods: Eight subjects (5 male, 3 female, mean age: 54, range: 48-62) with isolated medial meniscus tears due to an identifiable, traumatic injury that occurred prior to their study visit, were included in this study. Subjects were imaged using magnetic resonance imaging (MRI) to create 3D models of the femur, tibia, and articular cartilage. Subjects were then imaged using biplanar fluoroscopy while performing a quasi-static lunge from 0 to 105° of flexion. The 3D models of the knee were then registered to the biplanar fluoroscopic images to determine the *in vivo* motion and cartilage-to-cartilage contact strains within the joint (Figure 1). Subsequently, synovial fluid was collected from the subjects at the time of surgery (median time from injury to surgery: 13 weeks, range: 4-34 weeks). Matrix metalloproteinase (MMP) activity, sulfated glycosaminoglycan (sGAG), cartilage oligomeric matrix protein (COMP), prostaglandin E_2 (PGE2), and the collagen type II cleavage biomarker C2C were measured in the synovial fluid. Contact strains in the medial and lateral compartments in the uninjured and injured knee were compared as a function of flexion, using a two way repeated measures ANOVA. Spearman correlations were performed to determine the relationship between the average strain in the medial and lateral compartments at maximum flexion and the synovial fluid concentration of each biomarker.

Results: Peak cartilage contact strain in the medial compartment increased significantly in the injured knees compared to contralateral control knees ($p = 0.008$, Figure 2). Across all flexion angles, the average medial peak strain was 17% in the uninjured knees versus 23% in the injured knees. In the lateral compartment, the cartilage contact strain in the injured knee was significantly increased to 23% only at 105° of flexion ($p = 0.038$), compared to 17% in the uninjured knee. The average cartilage strain at maximum flexion positively correlated with total MMP activity (Figure 3) in the synovial fluid ($R = 0.79$, $p < 0.05$). However, there were no significant correlations between sGAG, COMP, PGE2, or C2C levels and cartilage strain in these subjects.

Conclusions: Cartilage contact strains increased after meniscal tear when compared to the contralateral uninjured knee, especially at higher flexion angles. In addition, total MMP activity positively correlated with the average cartilage strain across the joint. These findings suggest that the ability of the meniscus to distribute load is compromised after injury, thus overloading the cartilage and upregulating mechanically sensitive mediators like the MMPs. The increased strain and total MMP activity may reflect, or potentially contribute to, the early development of osteoarthritis that is observed following meniscal injury. These findings support the need to improve surgical treatment options following meniscal injury to restore normal cartilage loading.

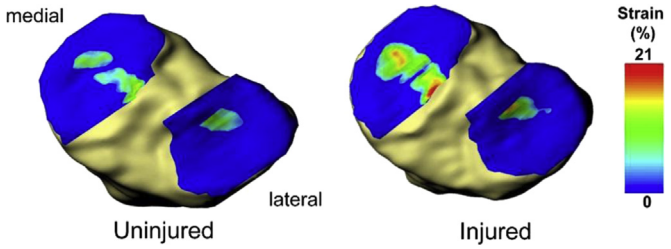

Figure 1. The strain maps are shown for one subject at 60° if flexion. The cartilage contact strain increased in the medial compartment of knees with a meniscus tear (right), as compared to the uninjured knee (left).

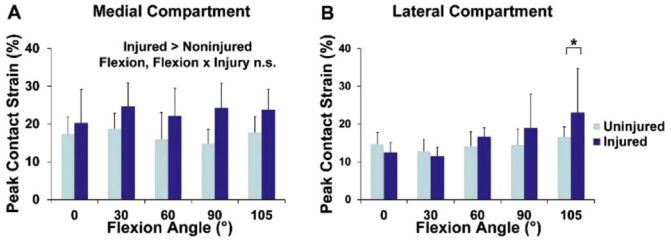

Figure 2**A**. In the medial compartment, meniscus injury increased peak contact strains. There were no statistically significant effects of flexion or interactions between flexion and injury. **B**. In the lateral compartment, a statistically significant interaction between flexion angle and meniscal injury was observed. At the maximum flexion angle of 105°, peak contact strains were increased in the injured knee as compared to the contralateral control.

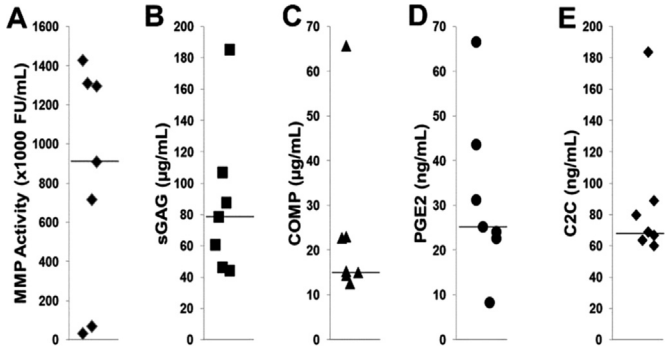

Figure 3. Synovial fluid concentrations of catabolic biomarkers in the knees of meniscal tear subjects at the time of surgery. (**A**) Matrix metalloproteinase (MMP) activity, (**B**) sulfated glycosaminoglycan (sGAG) concentrations, (**C**) cartilage oligomeric matrix protein (COMP) concentrations, (**D**) prostaglandin E_2 (PGE2) levels, and (**E**) C2C concentrations in the synovial fluid. Each point indicates the concentration for an individual and the median for each biomarker is indicated by the line.